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HLA MATCHING AT DNA LEVEL AND ITS IMPACT ON THE OUTCOME OF PEDIATRIC TRANSPLANTS FOR LEUKEMIA IN MULTI-RACIAL SINGAPORE

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We retrospectively reviewed the outcome of hematopoietic stem cell transplants (HSCT) in pediatric patients from a multi-racial background with acute and chronic leukemia based on the degree of HLA match at allelic/ DNA levels. We compared the rates of transplant related mortality (TRM), graft versus host disease (GVHD), relapse and overall survival (OS) in patients receiving related and unrelated donor HSCT with HLA match or mismatch donors. Between January 1998 and October 2010, 56 HSCT were performed in 52 patients whose median age was 110 (range, 12 – 226) months old. HLA match was defined as DNA match at 8 loci (HLA A, B, C and DRB1*). Matching at DNA level became standard from October 2004 and was available for 50 of the HSCT reviewed. For the 6 HSCT HLA typed prior to this time, related and unrelated donor HSCT were assigned as match and mismatch, respectively. HLA match grade of up to 4 alleles mismatches or a 1 antigen mismatch was acceptable. Amongst the 56 HSCT, indications included acute lymphoblastic leukemia (N = 20), acute myeloid leukemia (N = 21), acute biphenotypic leukemia (N = 4), chronic myeloid leukemia (N = 10) and juvenile myelomonocytic leukemia (N = 1). Of all the HSCT, *20* were *related* donor HSCT (11 bone marrow, 8 peripheral blood) and *36* were *unrelated* donor HSCT (19 bone marrow, 4 peripheral blood, 12 cord blood). At a median follow-up of 1.44 (0.02 – 10.75) years, the results are shown in the table.

Table 1. Results

				MMUD (N=25)	
Results (N=55)	MRD (N=17)	MMRD (N=3)	MUD (N=10) (9 ASC + 1 CB)	ASC (N=14)	CB (N=11)
TRM	6% (1/17)	0%	0%	0%	18% (2/11)
Acute GVHD grade 2 to 4	41% (7/17)	67% (2/3)	80% (8/10)	71% (10/14)	27% (3/11)
Chronic GVHD	18% (3/17)	67% (2/3)	50% (5/10)	57% (8/14)	27% (3/11)
Relapse	24% (4/17)	0%	0%	14% (2/14)	36% (4/11)
Overall Survival	76% (13/17)	67% (2/3)	100% (10/10)	71% (10/14)	82% (9/11)

*1 patient with missing data. MRD: matched related donor; MMRD: mismatched related donor; MUD: matched unrelated donor; MMUD: mismatched unrelated donor; ASC: adult stem cells (either bone marrow or peripheral blood stem cells); CB: cord blood

Two-thirds of our patients lack suitably matched related donors. Of all unrelated donor HSCT, 2/3 had HLA mismatch unrelated HSCT: excluding CB recipients; the TRM was low; GVHD rates were higher with correspondingly lower relapse rates compared to patients who received HLA match related donor HSCT. Patients who received HLA match unrelated donor typed at DNA level fare the best.

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DYSLIPIDEMIA FOLLOWING PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Children who receive solid organ transplants have been shown to frequently develop dyslipidemias after transplant due to the effect of immunosuppressive regimens on various lipid metabolism pathways. Little data exists to date, however, regarding the effect of hematopoietic stem cell transplantation (HSCT) on lipid profiles in the pediatric population, most of whom receive similar immunosuppressive therapies to their solid organ counterparts.
Methods: Baseline total cholesterol and triglyceride concentrations were collected just prior to transplant for 61 children who underwent HSCT between 2000 and 2009 at Lucile Packard Children's Hospital. Comprehensive lipid panels were then collected at each patient's annual post-transplant follow-up visit. Age at the time of transplant ranged from ten months to twenty years, and follow-up time ranged between one and nine years post-transplant. 59% of patients were male. Two patients required a second transplant. 74% of patients underwent allogeneic transplants; the remainder received autologous transplants. 55% of allogeneic recipients developed acute graft-versus-host disease (GVHD), and 36% developed chronic GVHD during their post-transplant course. Patients who developed GVHD were treated with steroids and a calcineurin inhibitor for an extended length of time.
Results: Mean pre-transplant total cholesterol concentrations were 136 mg/dL, below the 20th percentile for US children and adolescents. By four years post-transplant, triglyceride concentrations increased by 30% (to 130 mg/dL) and total cholesterol by 39% (to 189 mg/dL) from pre-transplant values. This total cholesterol concentration is above the 80th percentile for US children and adolescents. Between year one and year four post-transplant, low-density lipoprotein concentrations increased by 33% to 117 mg/dL, which is at the 85th percentile for US children and adolescents.
Conclusion: Dyslipidemias affect a significant proportion of pediatric HSCT recipients. This is likely due at least in part to immunosuppressive medications, particularly in those with GVHD requiring prolonged immunosuppressive treatment. The number of affected individuals increases with time since transplant, placing transplanted patients at increased risk for early cardiovascular disease. Further studies are necessary to determine if intervention, either pharmacologic or otherwise, is advisable for HSCT recipients in order to mitigate this increased risk.

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CORD BLOOD TRANSPLANTATION: 16 YEAR PEDIATRIC EXPERIENCE AT A SINGLE INSTITUTION

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Background: Cord blood is increasingly being used as an alternative stem cell source for hematopoietic stem cell transplantation (HSCT). We report the experience from a single institution and the impact of Center experience, improving supportive care, and increasing choice of cord units banked on outcome over time.
Methods: A retrospective chart review was performed reviewing all pediatric hematopoietic stem cell transplants over a 16 year period.
Results: Over a 16 year period 435 HSCT's were performed. Eighty of these were performed using cord blood as the stem cell source. Four were from related donors (RD) and 76 were from unrelated donors (URD). Twenty seven were transplanted for non-malignant diseases (NMD) (26 URD; 1 RD) and 53 with malignant disease (MD) (50 URD; 3 RD). Patients transplanted with related donors for malignant (3) and non-malignant (1) conditions had EFS and OS of 100% and 100% respectively. Incidence of acute GVHD grade II-IV was 50% and Grade III-IV was 0 with no chronic GVHD. Seventy-six patients were transplanted with unrelated donors using TBI and non-TBI containing regimens depending on disease. Immunosuppression for the majority (83%) consisted of CSA with

Table 1. Transplant Survival-Cord Blood

Survival	>100 Days	>1 Year	>3 YEars
Related EFS	100%	100%	100%
Related OS	100%	100%	100%
Unrelated (UR) EFS	67%	60%	61%
UR OS	68%	66%	61%
UR Malignant EFS	70%	63%	57%
UR Malignant OS	72%	67%	57%
UR Non-malig. EFS	62%	55%	52%
UR Non-malig. OS	62%	63%	61%
UR Malig. EFS after 2002	80%	74%	74%
UR Malig. OS after 2002	83%	79%	74%